October 4, 2019

Lin-Zhi International, Inc
Bernice Lin
VP Operations
2945 Oakmead Village Court
Santa Clara, CA 95051

Re: K192433
Trade/Device Name: LZI Methadone II Enzyme Immunoassay
Regulation Number: 21 CFR 862.3620
Regulation Name: Methadone test system
Regulatory Class: Class II
Product Code: DJR
Dated: August 30, 2019
Received: September 5, 2019

Dear Bernice Lin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm, Ph.D.
Acting Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
k192433

Device Name
LZI Methadone II Enzyme Immunoassay

Indications for Use *(Describe)*
The LZI Methadone II Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of methadone in human urine. The cutoff for both the qualitative and semi-quantitative modes of the assay is 300 ng/mL for methadone. The assay is designed for prescription use on automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative analytical chemistry method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Submitted On

August 30, 2019

Last Updated On

October 3, 2019

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter Name, Address, and Contact:

Lin-Zhi International, Inc.
2945 Oakmead Village Court
Santa Clara, CA 95051
Phone: (408) 970-8811
Fax: (408) 970-9030
e-mail: bclin@lin-zhi.com

Contact: Bernice Lin, Ph.D.
VP Operations

Device Name and Classification

Classification Name:	Enzyme Immunoassay, Methadone Class II, DJR (91 Toxicology), 21 CFR 862.3620
Common Name:	Homogeneous Methadone Enzyme Immunoassay
Proprietary Name:	LZI Methadone II Enzyme Immunoassay

Legally Marketed Predicate Device(s)

The LZI Methadone II Enzyme Immunoassay (EIA) is substantially equivalent to the Methadone Enzyme Immunoassay (k023317) manufactured by *Lin-Zhi International, Inc.* The LZI Methadone II Enzyme Immunoassay is identical or similar to its predicate in terms of intended use, method principle, device components, and clinical performance.

Device Description

The LZI Methadone II Enzyme Immunoassay is a homogeneous enzyme immunoassay with ready-to-use liquid reagents. The assay is based on competition between methadone in the sample and methadone labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the methadone concentration in the sample is measured in terms of enzyme activity. In the absence of methadone in the sample, methadone-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free methadone is present in the sample, antibody would bind to free methadone; the unbound methadone-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

The LZI Methadone II Enzyme Immunoassay is a kit comprised of two reagents, an R_1 and R_2, which are bottled separately but sold together within the kit.

The R_1 solution contains mouse monoclonal anti-methadone antibody, glucose-6-phosphate (G6P) nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (0.09 %) as a preservative. The R_2 solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with methadone in buffer with sodium azide (0.09 %) as a preservative.

Intended Use

The LZI Methadone II Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of methadone in human urine. The cutoff for both the qualitative and semi-quantitative modes of the assay is 300 ng/mL for methadone. The assay is designed for prescription use on automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative analytical chemistry method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

Comparison to Predicate Device

The LZI Methadone II Enzyme Immunoassay is substantially equivalent to the *Lin-Zhi International, Inc.* Methadone Enzyme Immunoassay, Calibrators, and Controls for Hitachi systems cleared by the FDA under the premarket notification k023317 for their stated intended use.

The following table compares the LZI Methadone II Enzyme Immunoassay with the predicate device.

Device Characteristics	**Subject Device** LZI Methadone II Enzyme Immunoassay	**Predicate Device (k023317)** Methadone Enzyme Immunoassay
Intended Use	The LZI Methadone II Enzyme Immunoassay is an in vitro diagnostic test intended for the qualitative and semi-quantitative determination of methadone in human urine. The cutoff for the qualitative and semi-quantitative modes of the assay is 300 ng/mL for methadone. The assay is designed for prescription use on automated clinical chemistry analyzers. The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures. ***The assay provides only a preliminary analytical result. A more specific alternative analytical chemistry method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***	The Lin-Zhi International, Inc. (LZI) Methadone Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of methadone in human urine at a cutoff value of 300 ng/mL. The assay is designed for professional use with a number of automated clinical chemistry analyzers. ***This assay provides a rapid screening procedure for determining the presence of methadone metabolite in urine. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.***
Analyte	methadone	methadone
Cutoff	300 ng/mL	300 ng/mL
Matrix	urine	urine
Calibrators Level	0, 150, 300, 600, and 1000 ng/mL	0, 150, 300, 600, and 1000 ng/mL
Controls Level	225 ng/mL and 375 ng/mL	225 ng/mL and 375 ng/mL
Storage	2-8ºC until expiration date	2-8ºC until expiration date

Performance Characteristics Summary:

Beckman Coulter® AU680 Analyzer

Precision

The assay tested in qualitative (ΔOD, mAU) and semi-quantitative (ng/mL) mode using a modified NCCLS-EP5 protocol. Methadone sample concentrations were prepared by spiking a methadone standard into a pool of negative human urine at concentrations ±25%, ±50%, ±75%, and ±100% of cutoff concentration.

Results shown below were obtained by testing all samples in replicate of two, two runs a day (one in the morning and one in the afternoon) for 22 days on one AU680 automatic clinical analyzer for a total of 88 runs. Samples were evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. One single lot of reagents, calibrators, and controls were used and stored at 2-8ºC when not in use.

Semi-Quantitative Precision Analysis Summary: Qualitative Results

Methadone Concentration	Within Run (N=22)	Total Precision (N=88)
	Qualitative Response	Qualitative Response
0 ng/mL	-	-
75 ng/mL	-	-
150 ng/mL	-	-
225 ng/mL	-	-
300 ng/mL	-	-
375 ng/mL	+	+
450 ng/mL	+	+
525 ng/mL	+	+
600 ng/mL	+	+

Semi-Quantitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Concentration	% of Cutoff	# of Samples	EIA Result	# of Samples	EIA Result
0 ng/mL	0.0%	22	22 Negative	88	88 Negative
75 ng/mL	25.0%	22	22 Negative	88	88 Negative
150 ng/mL	50.0%	22	22 Negative	88	88 Negative
225 ng/mL	75.0%	22	22 Negative	88	88 Negative
300 ng/mL	100.0%	22	18 Neg/4 Pos	88	66 Neg/22 Pos
375 ng/mL	125.0%	22	22 Positive	88	88 Positive
450 ng/mL	150.0%	22	22 Positive	88	88 Positive
525 ng/mL	175.0%	22	22 Positive	88	88 Positive
600 ng/mL	200.0%	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:

Beckman Coulter® AU680 Analyzer

Qualitative Positive/Negative Results:

300 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Methadone Concentration	**% of Cutoff**	**# of Samples**	**EIA Result**	**# of Samples**	**EIA Result**
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
75 ng/mL	25.0 %	22	22 Negative	88	88 Negative
150 ng/mL	50.0 %	22	22 Negative	88	88 Negative
225 ng/mL	75.0 %	22	22 Negative	88	88 Negative
300 ng/mL	100.0 %	22	17 Neg/ 5 Pos	88	59 Neg/29 Pos
375 ng/mL	125.0 %	22	22 Positive	88	88 Positive
450 ng/mL	150.0 %	22	22 Positive	88	88 Positive
525 ng/mL	175.0 %	22	22 Positive	88	88 Positive
600 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Linearity

To demonstrate linearity of the entire assay range, a drug free–urine pool spiked with methadone at 1000 ng/mL was serially diluted. Each sample was run in 10 replicates and the average was used to determine percent recovery compared to the expected target value.

Observed values were obtained and acceptable if measurements were ±15% of the expected values. Recovery values (Expected Value divided by the Observed Value) were considered acceptable between 85 – 115%.

Samples from the linear range of the assay (100 ng/mL to 1000 ng/mL) were tested with recovery ranging from 93.7% to 104.9%.

Expected Value (ng/mL)	Observed Value (ng/mL)	% Recovery
1000	950.5	95.0%
900	848.6	94.3%
800	767.9	96.0%
700	668.0	95.4%
600	572.2	95.4%
500	463.0	92.6%
400	393.4	98.4%
300	287.8	95.9%
200	187.4	93.7%
100	104.9	104.9%
20	15.8	78.9%
0	-7.1	N/A

Method Comparison - Clinical Samples

A total of ninety-four (94) unaltered clinical samples were tested with the LZI Methadone II Enzyme Immunoassay on the Beckman Coulter® AU680 automated clinical analyzer. Samples were evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in singlet.

All samples were confirmed with LC/MS for both methadone and methadone metabolite concentrations. Samples were collected by *Lin-Zhi International, Inc.* (LZI) and from the University of California, San Francisco (UCSF).

Semi-Quantitative Accuracy Study

Discrepant samples determined as compared to methadone concentration from LC/MS.

Candidate Device Results	**Negative**	**<50 % of Cutoff**	**Near Cutoff Negative** (between -50 % of cutoff to the cutoff)	**Near Cutoff Positive** (between cutoff and +50 % of cutoff)	**High Positive** (>50 % above cutoff)	**% Agreement**
Positive	0	0	1*	4	41	97.8 %
Negative	20	23	4	1**	0	97.9 %

Sample #	**LC/MS Methadone (ng/mL)**	**Pos/Neg Result**	**AU680 EIA Pos/Neg Result**
48*	274	-	+
50**	317	+	-

* Discrepant between 50% below cutoff and cutoff concentration (150 – 299.9 ng/mL)
** Discrepant between cutoff and 50% above cutoff concentration (300 – 449.9 ng/mL)

Qualitative Accuracy Study

Candidate Device Results	**Negative**	**<50 % of Cutoff**	**Near Cutoff Negative** (between -50 % of cutoff to the cutoff)	**Near Cutoff Positive** (between cutoff and +50 % of cutoff)	**High Positive** (>50 % above cutoff)	**% Agreement**
Positive	0	0	1*	4	44	97.8 %
Negative	20	23	4	1**	0	97.9 %

Sample #	**LC/MS Methadone (ng/mL)**	**Pos/Neg Result**	**AU680 EIA Qualitative Result (mAU)**	**Pos/ Neg Result**	**Qualitative Cutoff Rate (mAU)**
48*	274	-	176.5	+	133.5
50**	317	+	95.4	-	165.0

* Discrepant between 50% below cutoff and cutoff concentration (150 – 299.9 ng/mL)
** Discrepant between cutoff and 50% above cutoff concentration (300 – 449.9 ng/mL)

Cross-reactivity

The Cross-reactivity of various potentially interfering drugs were tested by spiking various concentrations of each substance into a pool of negative human urine and then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

The table below lists the concentration of each test compound that gave a response approximately equivalent to that of the cutoff calibrator (as positive) or the maximal concentration of the compound tested that gave a response below the response of the cutoff calibrator (as negative). Compounds tested at high concentration with results below the cutoff value were listed as Not Detected (ND).

Methadone and Structurally Related Compounds:

Compound	Target Concentration (ng/mL)	% Cross-reactivity
Methadone	300	100.00%
EDDP	100,000	<0.30%
EMDP	100,000	<0.30%
(-)-α-Noracetylmethadol (Nor-LAAM) HCl	75,000	0.40%
LAAM HCl	25,000	1.20%
(±)-α-Methadol	26,500	1.13%
(-)-Isomethadone HCl	35,000	0.86%

Structurally unrelated compounds were additionally spiked into pooled negative human urine to desired concentrations (as described above). These solutions were then split into three portions; one without methadone, and the remaining two that were further spiked with methadone standards to a final methadone concentration of 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25% cutoff concentration, respectively). Samples were then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

Structurally Unrelated Pharmacological Compounds:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Acetaminophen	100,000	ND	Neg	Pos
6-Acetylmorphine	100,000	ND	Neg	Pos
Acetylsalicylic Acid	100,000	ND	Neg	Pos
Amitriptyline	100,000	ND	Neg	Pos
Amlodipine Besylate	100,000	ND	Neg	Pos
Amoxicillin	100,000	ND	Neg	Pos
d-Amphetamine	100,000	ND	Neg	Pos
Atorvastatin	100,000	ND	Neg	Pos
Acetaminophen	100,000	ND	Neg	Pos
6-Acetylmorphine	100,000	ND	Neg	Pos

Structurally Unrelated Pharmacological Compounds, continued:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Acetylsalicylic Acid	100,000	ND	Neg	Pos
Amitriptyline	100,000	ND	Neg	Pos
Amlodipine Besylate	100,000	ND	Neg	Pos
Amoxicillin	100,000	ND	Neg	Pos
d-Amphetamine	100,000	ND	Neg	Pos
Atorvastatin	100,000	ND	Neg	Pos
Benzoylecgonine	100,000	ND	Neg	Pos
Buprenorphine	100,000	ND	Neg	Pos
Bupropion	100,000	ND	Neg	Pos
Caffeine	100,000	ND	Neg	Pos
Carbamazepine	100,000	ND	Neg	Pos
Cetirizine	100,000	ND	Neg	Pos
Chlorpheniramine	100,000	ND	Neg	Pos
Chlorpromazine	100,000	ND	Neg	Pos
Clomipramine	100,000	ND	Neg	Pos
Codeine	100,000	ND	Neg	Pos
Desipramine	100,000	ND	Neg	Pos
Diphenhydramine	100,000	ND	Neg	Pos
Duloxetine	50,000	ND	Neg	Pos
Fentanyl	100,000	ND	Neg	Pos
Fluoxetine	100,000	ND	Neg	Pos
Fluphenazine	100,000	ND	Neg	Pos
Gabapentin	100,000	ND	Neg	Pos
Hydrocodone	100,000	ND	Neg	Pos
Hydromorphone	100,000	ND	Neg	Pos
Ibuprofen	100,000	ND	Neg	Pos
Imipramine	100,000	ND	Neg	Pos
Lisinopril	100,000	ND	Neg	Pos
Losartan	100,000	ND	Neg	Pos
Loratidine	100,000	ND	Neg	Pos
MDA (3,4-methylenedioxy-amphetamine)	100,000	ND	Neg	Pos
MDEA	100,000	ND	Neg	Pos
MDMA (3,4-methylenedioxy-methamphetamine)	100,000	ND	Neg	Pos
Meperidine	100,000	ND	Neg	Pos
Metformin	100,000	ND	Neg	Pos
Metoprolol	100,000	ND	Neg	Pos
d-Methamphetamine	100,000	ND	Neg	Pos
Morphine	100,000	ND	Neg	Pos
Nicotine	100,000	ND	Neg	Pos
Nortriptyline	100,000	ND	Neg	Pos
Omeprazole	100,000	ND	Neg	Pos

Structurally Unrelated Pharmacological Compounds, continued:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Oxazepam	100,000	ND	Neg	Pos
Oxycodone	100,000	ND	Neg	Pos
Oxymorphone	100,000	ND	Neg	Pos
Phenobarbital	100,000	ND	Neg	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	ND	Neg	Pos
Quetiapine	100,000	ND	Neg	Pos
Ranitidine	100,000	ND	Neg	Pos
Salbutamol (Albuterol)	100,000	ND	Neg	Pos
Sertraline	100,000	ND	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	100,000	ND	Neg	Pos
L-Thyroxine	100,000	ND	Neg	Pos
Tramadol	100,000	ND	Neg	Pos
Zolpidem	100,000	ND	Neg	Pos

Endogenous Compound Interference:

Endogenous compounds were spiked into pooled negative human urine to desired concentrations. These solutions were then split into three portions; one without methadone, and the remaining two that were further spiked with methadone standards to a final methadone concentration of 225 ng/mL or 375 ng/mL (as negative or positive controls, ±25% cutoff concentration, respectively). Samples were then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

Endogenous Substance	Concentration Tested (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Acetone	1000	Neg	Neg	Pos
Ascorbic Acid	1500	Neg	Neg	Pos
Bilirubin	2	Neg	Neg	Pos
Boric Acid*	1000	Neg	Neg	Neg
Calcium Chloride (CaCl2)	300	Neg	Neg	Pos
Citric Acid (pH 3)	800	Neg	Neg	Pos
Creatinine	500	Neg	Neg	Pos
Ethanol	1000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
γ-Globulin	500	Neg	Neg	Pos
Glucose	3000	Neg	Neg	Pos
Hemoglobin	300	Neg	Neg	Pos
β-hydroxybutyric Acid	100	Neg	Neg	Pos
HSA	500	Neg	Neg	Pos

Endogenous Compound Interference, continued:

Endogenous Substance	Concentration Tested (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	225 ng/mL Control	375 ng/mL Control
Oxalic Acid	100	Neg	Neg	Pos
Potassium Chloride*	6000	Neg	Neg	Neg
Riboflavin	0.3	Neg	Neg	Pos
Urea	6000	Neg	Neg	Pos
Uric Acid	10	Neg	Neg	Pos
Sodium Azide	1000	Neg	Neg	Pos
Sodium Chloride	1000	Neg	Neg	Pos
Sodium Fluoride	1000	Neg	Neg	Pos
Sodium Phosphate	300	Neg	Neg	Pos

The following endogenous compounds which showed interference at ±25 % of cutoff concentrations were then spiked into negative urine and at ±50 % of cutoff concentrations (150 ng/mL and 450 ng/mL) for the assay.

Interference was observed with Boric Acid at 1 % w/v. No other significant undesired cross-reactants or endogenous substance interference was observed.

Endogenous Substance	Concentration Tested (ng/mL)	Spiked Methadone Concentration		
		0 ng/mL	150 ng/mL Control	450 ng/mL Control
Boric Acid	1000	Neg	Neg	Neg
Potassium Chloride	6000	Neg	Neg	Pos

Specific Gravity:

Samples ranging in specific gravity from 1.003 to 1.028 were split into three portions each and either left un-spiked or further spiked to a final methadone concentration of either 225 ng/mL or 375 ng/mL (the negative and positive control concentrations, respectively). These samples were then evaluated in qualitative mode. No interference was observed.

pH Interference Study:

Negative urine and urine spiked with methadone to the final methadone concentration of either 225 ng/mL or 375 ng/mL (the negative and positive control concentrations, respectively) were adjusted to the following pH levels and tested by the assay. The pH adjusted solutions were evaluated against the cutoff calibrator.

No major interference between pH 3 to pH 11. Results are summarized in the following table:

pH	Spiked Methadone Concentration		
	0 ng/mL	225 ng/mL Control	375 ng/mL Control
pH 3	Neg	Neg	Pos
pH 4	Neg	Neg	Pos
pH 5	Neg	Neg	Pos
pH 6	Neg	Neg	Pos
pH 7	Neg	Neg	Pos
pH 8	Neg	Neg	Pos
pH 9	Neg	Neg	Pos
pH 10	Neg	Neg	Pos
pH 11	Neg	Neg	Pos

Summary:

The information provided in this pre-market notification demonstrates that the LZI Methadone II Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its general intended use. Substantial equivalence was demonstrated through comparison of intended use and physical properties to the commercially available predicate device as confirmed by chromatography/mass spectrometry (LC/MS), an independent analytical chemistry method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Methadone II Enzyme Immunoassay is safe and effective for its stated intended use.